

# Some Clinical and Pathological Features of a Case of Tuberculous Meningitis

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THIS case is considered to be of interest because of the pathological findings and of the problem of diagnosis presented by the signs and symptoms.

The patient was an unmarried woman aged 24. There was nothing relevant in the family history. Apart from pleurisy with effusion six months before admission, there was no history of any previous serious illness.

Early in December, 1945, intermittent 'numbness' of the right index finger was noticed. A week or two later this feeling began to appear in the right upper and lower limbs. It lasted about fifteen minutes at a time and recurred several times a day. In January, 1946, she noticed a tendency to trail the right foot, and found that the right hand was becoming clumsy and useless; for example, writing and buttoning clothes became very difficult.

Towards the end of January, in addition to the numbness in the arm and leg, there were attacks of pain in the right side of the face and head. She described this as being neuralgic in character. About the same time there was occasional vomiting. On 4th February she was admitted to hospital.

Following admission the condition improved; vomiting ceased and the temperature remained normal. Then suddenly on the 24th February there was a rise in temperature accompanied by headache, vomiting, photophobia and some neck rigidity. The cerebro-spinal fluid was found to be under increased pressure, but was otherwise normal. On 3rd March she was transferred to the Royal Victoria Hospital.

On examination there was no evidence of clouding of consciousness. On the contrary, she was exceptionally lucid and alert, and the impression was of a person well above average intelligence giving accurate responses to questions and sensory tests. There was no dysphasia.

The temperature was 99.8 and the pulse rate 110. There was slight neck rigidity and photophobia.

Examination of cranial nerve functions showed no impairment of the visual fields, and the discs and fundi were normal. The pupils were equal, central, and reacted to light and on accommodation. Lateral nystagmus was present, most marked on looking to the right. The functions of the remaining cranial nerves were normal. Tests for muscle-joint sense and for sensibility to vibration, touch, pain, and temperature showed no abnormality. There was no astereognosis.

The right upper limb showed some loss of tone associated with intention tremor, dysmetria, inability to carry out rapidly alternating movements, and slight weakness of grip in the right hand. The right lower limb showed slight generalised weakness, most marked in the dorsi-flexors of the foot, associated with a small degree of inco-ordination of movement. The left upper and lower limbs showed no motor abnormality. The tendon reflexes in the right upper and lower limbs were increased and the abdominal and plantar reflexes on the right side were indefinite. On the

left side all reflexes were normal. There was no history of any disturbance of the vesical or bowel sphincters.

The following investigations were carried out: X-ray of the skull and chest showed no abnormality. The white-cell count was 8,600 per c.mm. The blood sedimentation rate was 50 mm. in one hour (Westergren).

Lumbar puncture was performed on 5th March. The cerebro-spinal fluid pressure was 250 mm. water. There were 270 cells per c.mm., of which 70 per cent. were polymorphs. The protein was 210 mg. per cent. and the chlorides 680 mg. per cent. No organisms were found. (Cultures of the cerebro-spinal fluid for tubercle bacilli showed no growth at the end of six weeks.)

#### SUMMARY OF CLINICAL FINDINGS.

The patient had had a pleural effusion six months before admission, and gave a history of sensory Jacksonian fits of three months' duration, suggesting a lesion in the left parietal region. There were two recent attacks of headache and vomiting, with slight neck rigidity and photophobia.

There were marked signs of cerebellar dysfunction all referred to the right side: hypotonia, impairment of rapidly alternating movements, intention tremor, dysmetria, and nystagmus. The sensory fits suggested a lesion in the left parietal region, and there was slight weakness of the right upper and lower limbs, with increased tendon reflexes and indefinite superficial reflexes on the right side. There were no objective sensory changes, no astereognosis, and no dysphasia. The cerebro-spinal fluid was under increased pressure (250 mm.) and contained 270 cells per c.mm. (70 per cent. polymorphs), 210 mg. protein, and 680 mg. chlorides per cent.

The possibility of tuberculous meningitis was considered, especially in view of the recent history of pleurisy and the unclouded mental state. The high cell content of the cerebro-spinal fluid with numerous polymorphs, together with focal signs, however, suggested the possibility of abscess. But localisation was obviously difficult. How could one reconcile the history of sensory fits which might be related to the left parietal cortex with the signs, on examination, which pointed to a right-sided cerebellar lesion? The complete absence of any difficulty related to stereognosis was striking, as was also, in a lesser degree, the absence of any dysphasia.

It was decided that it was impossible to exclude the possibility of abscess, and on 6th of March needling of the left parietal region and of the cerebellum was carried out, in both cases with negative results. Air ventriculography performed at the time of operation showed no abnormality.

Following operation, the patient's condition remained unchanged for several days. Consciousness continued bright. On 9th March the cerebro-spinal fluid contained 60 cells per c.mm. (equal numbers of lymphocytes and polymorphs), 149 mg. protein, and 610 mg. chlorides per 100 c.c. On that day (9th March) deterioration set in. Consciousness became clouded, gradually deepening to coma, and death took place on 15th March.

#### POST-MORTEM FINDINGS.

At post-mortem the brain was slightly swollen, with flattening of the convolutions. At the base of the brain there was a well-marked thick exudate. Over the vertex on the left side, just posterior to the Rolandic fissure, there was marked fibrous thickening of the meninges over an area about 1.5 cm. in the longest diameter. Towards the periphery of the fibrosed area a few yellowish-white nodules about 1 mm. in diameter were visible.

Direct examination of the exudate at the base of the brain showed the presence of tubercle bacilli.

On section of the brain after fixation, a yellowish-white nodule measuring just over 1 cm. in diameter was found lying deep in the post-central gyrus. Smaller areas were recognisable along the sulcus, and the infection appeared to spread towards the surface to reach the area of thickening in the meninges. There was slight dilatation of the ventricular system, and the ependymal lining was noted to be granular.

Histologically, the lesion was found to consist of an area of caseous necrosis involving both meninges and brain tissue. Towards the margin there was definite tubercle formation with aggregates of large mononuclears, lymphocytes, and giant cells.

The meninges showed much fibrous thickening, and even here tubercle formation and giant cells were common. The appearances were those of a slowly progressive lesion which had eventually ruptured into the sub-arachnoid space.

At the base of the brain the meningeal exudate was much more fulminant and acute. There was no tubercle formation. Polymorphs and large mononuclears were present, and there was marked exudation of fibrin and widespread caseation. The necrosis involved the blood-vessel walls; this had led to softening of the adjacent brain tissue. There was also slight extension of the infection along the perivascular space.

The wall of the lateral ventricle showed patchy loss of the lining cells, with swelling and oedema of the underlying tissue. There were also focal infiltrations of lymphocytes and large mononuclears. This ependymitis was believed to be the result of backwash of infected cerebro-spinal fluid into the ventricles.

Post-mortem examination of the rest of the body was not permitted. There was, however, no clinical evidence of miliary tuberculosis. The brain showed no other lesions on multiple section.

#### RELATIONSHIP OF SYMPTOMS TO LESION.

The anatomical representation of the body on the sensory cortex of the post-central convolution is generally stated to follow that of the corresponding motor area. On this assumption, the order of spread of a sensory Jacksonian fit should be from the toes upwards over the leg to the hip, and thence to the shoulder, arm, fingers, and face. In the case under discussion one would have expected the paræsthesiæ which began in the fingers to spread simultaneously to the face and forearm. In fact, the extension was first to the forearm, arm, and lower limb, the

face only being involved several weeks later. Sittig,<sup>2</sup> in a clinical study of sensory Jacksonian fits, has described ten otherwise typical cases in which the spread of the attacks did not correspond to the accepted anatomical localisation. He refers to Head's assumption, "that there is a representation or 'schema' of the body on the brain; . . . this is not a fixed or pre-formed localisation, but rather a nervous structure which is especially often thrown into action, a pattern or a frequently employed functional mechanism." Sittig also refers to the researches of Leyton and Sherrington on anthropoids, in which they found that the same point of the electrically excitable cortex gives different reactions according to different sequences of stimulation, i.e., whether the stimulus is moved from above downwards, or inversely. He concludes that varying orders of spread of sensory Jacksonian fits are determined by the intensity of the stimulus: "If the excitation is slight, only a quite limited part of the body is affected, as the thumb and index finger; while if it is stronger, the excitation extends, and may follow a pre-formed functional pattern in the 'schema' or some other functional mechanism."

The disorders of tone and movement, which were most marked in the right upper limb, made it seem probable that there was a right-sided cerebellar lesion. Post-mortem examination of the brain showed that the only focal lesion was in the left parietal region, and these symptoms must have resulted from this lesion.

It is, of course, accepted that cortical lesions can cause disorders of movement and of tone. Head<sup>2</sup> states: "Any lesion which disturbs postural schemata will interfere with static tone. For, in order that a part of the body at rest may retain a normal posture, afferent postural impulses must exert a constant influence on the activity of the appropriate receptive centres of the cortex. These are the repository of spacial schemata. The physiological changes brought about by this stream of afferent impressions not only checks and controls voluntary movement, but ensures that the static tone of the part shall be adapted to maintain its position. Consciousness is in no way necessary for such co-ordination; in fact, the regulation of tonic innervation occurs entirely on the physiological level. Any lesion, which tends to destroy postural schemata, not only disorders voluntary movement, but under suitable conditions may diminish static tone."

In the case under discussion muscle-joint sense and the sensation of touch were not impaired, and the faculty of stereognosis was not in any way diminished. It is of interest here that these functions should have been left undamaged by a lesion which produced the degree of ataxia and hypotonia described, in addition to sensory Jacksonian fits of considerable extent.

#### PATHOLOGY.

Because of the frequent association of the two conditions, it was formerly believed that tuberculous meningitis was merely the meningeal manifestation of miliary dissemination. Rich was one of the first to point out that this was not so in the majority of cases. He considered that the lesion most commonly responsible for tuberculous meningitis is a focal plaque occurring either in the meninges or in the underlying brain. He believed that such foci originated as the result of a

bacteraemia occurring either during the primary infection or during a post-primary progressive infection. The resulting lesions (of which the one described in this case is an example) are in effect solitary tuberculomata in contact with the meninges, into which the organisms escape. If the number of organisms is small and the resistance good, the meningitis may remain localised, resulting merely in fibrosis and adhesion of the overlying meninges. An attempt at such a process was seen here. More often a generalised diffuse meningitis results, and perhaps due to some gravity effect, the exudate is most plentiful at the base of the brain.

The claim that it is these foci, and not miliary tuberculosis, which are responsible for the development of meningitis has been supported by both clinical and experimental work. Injection of large numbers of tubercle bacilli directly into the bloodstream of both normal and hypersensitive animals frequently results in miliary tuberculosis. Meningitis does not occur in these animals unless they develop a focal tuberculoma adjacent to the meninges. This is regarded as proof that meningitis does not develop from escape of bacilli directly into the meninges from the blood stream.

Clinically, miliary tuberculosis is much more common than tuberculous meningitis, and about 20 per cent. of the latter occur in cases without any miliary spread. Further, in many cases in which both conditions are found the histological age of the lesions differs; in fact, it has even been shown that in some cases the meningitis may be the origin of the miliary spread. Therefore, even when the two conditions co-exist, it should not be hastily assumed that their origin was simultaneous, or that the miliary lesions were the initiating factor in the meningitis.

Rich analysed eighty-two human cases of tuberculous meningitis, and found focal caseous lesions older than the meningitis in seventy-seven. Similar findings have subsequently been reported by other workers.

This case is regarded as being a classical example of the origin of meningitis from a focal tuberculous lesion in contact with the meninges. The appearances of the tuberculoma suggest that it had been present for several months. The situation in the left post-Rolandic area is such as to explain the focal nature of the original symptoms. The gradual extension of these symptoms would appear to be related to slow leakage of organisms over the adjacent cortex. When the lesion finally discharged into the sub-arachnoid space, there had been time for multiplication of organisms, and suitable conditions had been established for the development of a fulminating terminal meningitis.

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2. SITTING, OTTO: *Brain*, 1925, 48, 233.
3. HEAD, HENRY: *Studies in Neurology*, London, 1920, p. 724.

SOME CLINICAL AND PATHOLOGICAL FEATURES OF  
A CASE OF TUBERCULOUS MENINGITIS

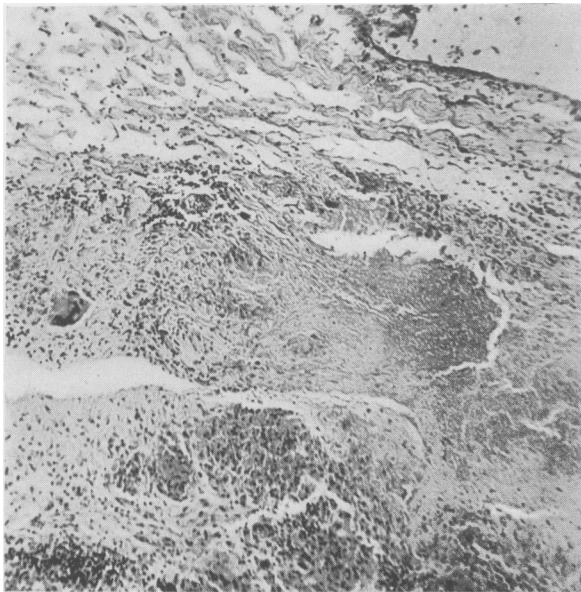


FIG. 1 (x 120)

The "Rich Focus" in the post-central sulcus, involving both brain and meninges. It consists of an area of caseation surrounded by small tuberculous follicles and fibrosed meninges.

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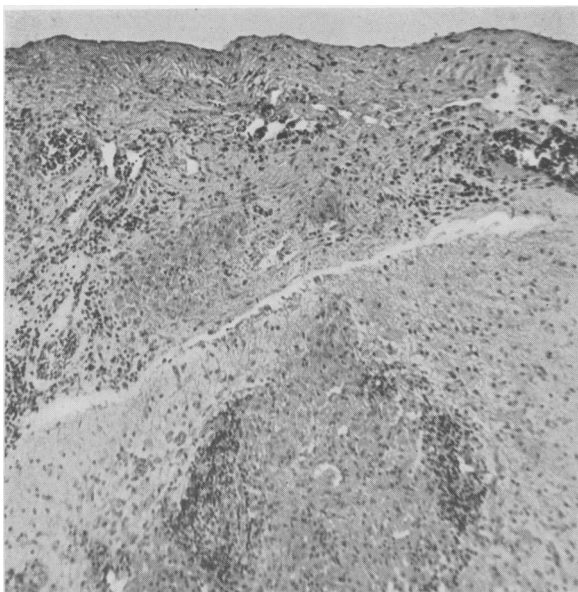


FIG. 2 (x 120)

To show the gross fibrosis of the meninges overlying the affected sulcus. The recent extension of the tuberculous process can be seen in the underlying cortex.

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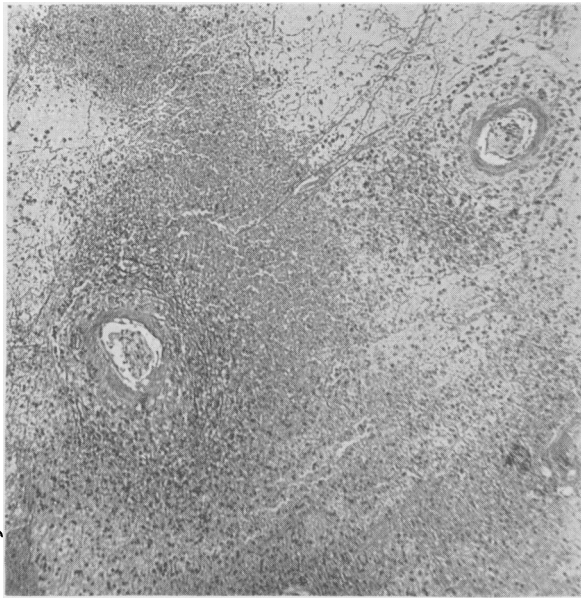


FIG. 3 (x 120)

Showing the fulminant type of reaction at the base of the brain. There is widespread caseation, involving vessel walls, and exudation of fibrin. Many polymorphs are present. Note the absence of tubercle formation.

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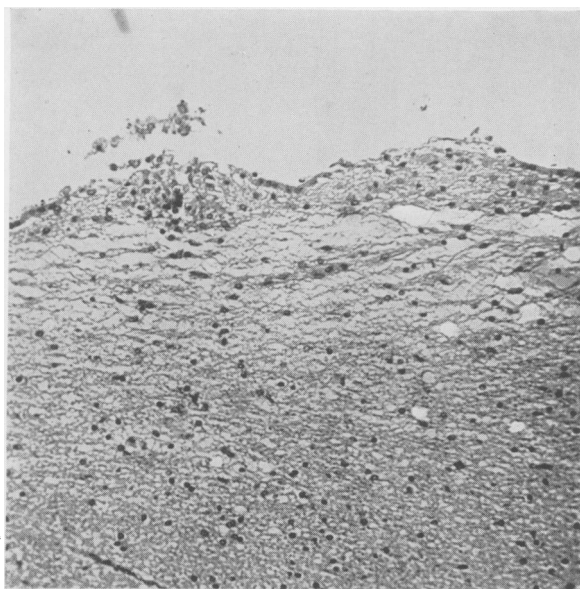


FIG. 4 (x 150)  
Ventricular walls showing loss of ependymal cells,  
infiltration by mononuclear cells, and œdema of the  
deeper tissues.

*Photographs by Mr. David Melfaffey, A.R.P.S.*